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10/781,928	02/20/2004	Connie Li Sun	034536-0829	9693

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EXAMINER	
TUCKER, ZACHARY C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,928	SUN ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *3-5 and 8-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

A Requirement for Restriction in the instant application was mailed 25 November 2005. Applicant's election without traverse of the invention of Group I, imidazopyrazines compounds, in the reply filed on 27 December 2005 is acknowledged.

In the Requirement for Restriction letter, there was a further requirement for applicant to elect a single disclosed species from which examination of the elected Group will begin, for searching purposes. In response to this requirement, applicant has indicated the compound of Example 31, page 77 of the instant specification, named cyclopropyl-(3-phenyl-imidazo[1,2-a]pyrazine-8-yl)-amine. The election of this species was made **with** traverse. The ground for traversal was explained as being for the reason that "all of the compounds of group II fall within structurally similar subclasses, and that searching the subclasses should not place a serious burden on the Examiner." Group II of the Requirement for Restriction, contrary to the traversal statement, is not composed of claims drawn to compounds, the claims of that Group are drawn to methods of treating diseases and conditions, and a pharmaceutical composition for that purpose. Claims of Group II are additionally in completely different class and subclass than the elected claims, drawn to the chemical compounds *per se*. Since the election of Group I over Group II was clearly made without traverse, and Group II is not drawn to chemical compounds, the remarks pertaining to Group II in reference to the additional requirement to elect a single disclosed species for examination are not understood.

In the Requirement for Restriction letter, it is explained that a reply to the requirement to elect a single disclosed species for examination must include a listing of all claims readable thereon, which listing was not provided with applicants' remarks in the reply. Because the reply appears to have been made in good faith, this omission will be overlooked. Claims 1, 2, 6 and 7 are readable on the elected species, as determined by the examiner. A search of the prior art, starting with all compounds of Claims 1, 2, 6 and 7 wherein one of R_1 and R_2 is H and the other is cyclopropyl; R_3 and R_4 are both H and R_5 is an optionally substituted phenyl ring (R_6 must always be H, as defined in the claims) was undertaken. No compounds according to the initial search were found in the prior art; compounds of that genus are therefore deemed novel and unobvious. When the search was expanded in the interest of finding prior art disclosures disclosing or suggesting chemical compounds wherein one of R_1 and R_2 is H and the other is *any* of the permitted substituents, R_3 and R_4 are both H and R_5 is an optionally substituted phenyl ring, prior art suggesting such compounds was found, whereupon the search was stopped. No claim in the application has been completely searched; allowable species are indicated in the section *infra* headed "Allowable Subject Matter."

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 6 and 7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, and 14 of copending Application No. 10/845,586. Although the conflicting claims are not identical, they are not patentably distinct from each other at least for the reason that several cyclopropylamine-based compounds named in claim 14 of the copending application are embraced by, that is, anticipate instant claims 1 and 2. Since the copending application is a continuation-in-part of the instant application, it is presumed that the disclosures are substantially similar, and therefore that the species named in instant claims 6 and 7 are disclosed in or are obvious over the species disclosed in the specification of the copending application, so that said species specified in instant claims 6 and 7 are obvious over the generic claims in the copending application, when those generic claims are interpreted in light of the disclosure of the copending application. It is permissible to rely on the specification of a patent or copending application as a dictionary to define elements of the claimed invention in said patent or copending application (MPEP § 804 II, B). In the instant case, the specification would

define the genera according to claims 1-3 of the copending application as including certain of the species recited in instant claims 6 and 7. Should applicants disagree with this conclusion, this is an invitation to provide evidence for patentable distinctness of the claims of the copending application over the claims of the instant application.

For example, in claim 14, the last named compound on page 231 of the copending application, N-[4-(8-cyclopropylamino-imidazo[1,2-a]pyrazine-3-yl)-phenyl]-methanol, is a compound according to instant claims 1 and 2 wherein R_1 is H, R_2 is cyclopropyl, R_3 and R_4 are both H and R_5 is phenyl, substituted with an alkyl group. The compound named in section [0329] if the copending application is a positional isomer of 3-(8-cyclopropylamino-imidazo[1,2-a]pyrain-3-yl)-phenol, specified in instant claims 6 and 7. The two compounds named in sections [0357] and [0358] of the copending application are indeed specified in instant claims 6 and 7, and are set forth in the specification of the copending application among the preferred compounds of formula (I), as is set forth in sections [0039] and [0040] therein.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first and second paragraphs of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation of the compounds named in those two claims, and pharmaceutically acceptable salts thereof, does not reasonably provide enablement for the full scope of all prodrugs of the named compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the full scope of the invention specified in instant claims 6 and 7.

The Wands factors provide a guide for determining the scope of enablement provided by a given disclosure:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

(A) Though it might appear that the scope of instant claims 6 and 7 is limited only to simple derivatives of the named compounds, embraced the structure diagrams depicted in the specification, as will be apparent from the following, it is not. A prodrug, as defined by Bundgaard in:

Hans Bundgaard, Design of Prodrugs, page 1. © 1985 Elsevier Science Publishers.

"is an inactive species, and therefore, once its job is completed, intact prodrug represents unavailable drug." Thus, an important requirement of prodrugs of

compounds named in claims 6 and 7 is that they be pharmacologically inactive. Prodrugs come in myriad forms, and are not limited only to ester and polypeptide derivatives, which are suggested as preferred types in sections [0092] and [0093] of the instant specification. A prodrug may be an amide, a Mannich base (imine), an acyclic precursor to a cyclic compound, a compound of the drug covalently or ionically bound to another drug with different action or a carboxylic acid which is decarboxylated to provide the active drug or a complex with a synthetic polymer, to name several.

So, the scope of all prodrugs is quite broad. A prodrug does not necessarily depend on the identity of the pharmacologically active agent formed from the prodrug upon metabolism for patentability. A prodrug is not necessarily even structurally related to the compound of which it is a prodrug, since the metabolism *in vivo* of that compound is what provides the active drug.

(B) Prodrugs of the compounds named in claims 6 and 7 are the nature of the invention.

(C) The state of the prior art with respect to the development of prodrugs is represented by:

> Richard B. Silverman, The Organic Chemistry of Drug Design and Drug Action, pages 352-400. © 1992 Academic Press, Inc.

Silverman teaches many kinds of prodrugs, including all of the types mentioned above in section "(A)." Pages 353 and 354 list eight various reasons why a prodrug would be desirable. On page 354, Silverman teaches that some prodrugs are discovered accidentally, and some designed on the basis of known metabolic transformations.

(D) The level of ordinary skill in the art is that of a medicinal chemist, holding a graduate level degree in the field and with experience in preparative organic chemistry.

(E) As discovery of prodrugs is sometimes accidental, then it follows that whether a given compound will function as a prodrug or not is sometimes unpredictable. On the other hand, when a compound is designed as a prodrug, one must first understand the metabolic milieu into which the presumptive prodrug is to be introduced, and must also know to what extent the compound will be metabolized. The metabolism of xenobiotics in animals and humans is not always predictable. A prodrug must also, by definition, be pharmacologically inactive, so one must know which modifications of the structure of the parent compound will render it inactive. Structure-activity relationships must in large part be determined empirically, although once a rule is discerned, the structure-activity of a given series of compounds becomes predictable.

Theoretically, if one of ordinary skill in the art knew all of the above variables, prodrug structure could be predicted in advance. The reality is that all of these considerations, in total, must be empirically derived when the compound in question is an allegedly novel compound, as are compounds according to claims 6 and 7. On balance, all of these factors taken together render the planned and directed development of prodrugs practically unpredictable

(F) The following passages are the total extent of direction provided in the specification pertaining to prodrugs of compounds according to the instant inventoin. –

[0092] The compound of Formula (I) may also act as a prodrug. A "prodrug" refers to an agent which is converted into the parent drug in vivo. Prodrugs are often useful because, in some situations, they may be easier to administer than the parent drug. They may, for instance, be bioavailable by oral administration whereas the parent drug is not. The prodrug may also have improved solubility in pharmaceutical compositions over the parent drug. An example, without limitation, of a prodrug would be a compound of the present invention which is administered as an ester (the "prodrug") to facilitate transmittal across a cell membrane where water solubility is detrimental to mobility but then is metabolically hydrolyzed to the carboxylic acid, the active entity, once inside the cell where water solubility is beneficial.

[0093] A further example of a prodrug might be a short polypeptide, for example, without limitation, a 2 - 10 amino acid polypeptide, bonded through a terminal amino group to a carboxy group of a compound of this invention wherein the polypeptide is hydrolyzed or metabolized in vivo to release the active molecule. The prodrugs of a compound of Formula (I) are within the scope of this invention.

No metabolic studies of the compounds *in vivo* have been done and no structure-activity rules are outlined – certainly no teaching as to which modifications will afford an *inactive* compound is found in the specification. The specification does not specifically address any type of prodrug other than acylated derivatives.

(G) No working examples, out of the 128 preparative examples, of any prodrug are in the disclosure.

(H) In order for one of ordinary skill in the art to practice the full scope of the prodrugs of compounds according to claims 6 and 7, a complete structure activity analysis of *all* of the named compounds would have to be completed. This analysis

would involve hundreds of individual compounds. The practitioner would first screen for which type of modifications of the molecular structure would render an inactive compound. Then, metabolic studies of all of the *inactive* derivatives of the compounds would have to be completed, and compounds that are converted to a compound according to claims 6 and 7 upon metabolism *in vivo* identified. This research would potentially be inconclusive and could take years. Additionally, one of ordinary skill in the art would necessarily have to undertake an effort to make totally new classes of compounds not bearing any structural similarity to the compounds named in claims 6 and 7, such as procyclic compounds converted to heterocyclic compounds (in the instant case, imidazo[1,2-a]pyridine compounds) *in vivo*, which are mentioned on page 360 of Silverman. Investigations of polymer-bound forms of the compounds according to claims 6 and 7 would be necessary also. Because of the fact that in different animals, xenobiotics are metabolized differently because they are acted upon by different enzymatic pathways, this effort would have to be duplicated in each species for which a prodrug were sought, for each compound. As evidence that animals will differ substantially in the manner that xenobiotics are metabolized, the examiner presents:

> Al-Dabbagh and Smith, "Species differences in oxidative drug metabolism: some basic considerations." Archives of toxicology. Supplement. Archiv fur Toxikologie. supplement, vol. 7, pages 219-231 (1984).

Al-Dabbagh and Smith states that the metabolic process itself is highly variable both between and within animal species, and that the toxic effect of many chemicals is a function of how the chemical is metabolized rather than the substance itself.

Given the amount of direction in the disclosure, the amount of experimentation required to realize the full scope of instant claims 6 and 7 is clearly undue. Applicants

have not described the manner and process of making prodrugs of compounds according to claims 6 and 7, in such full, clear, concise, and exact terms as to enable any person skilled in the art to do so.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons explained in the following.

The term "protected hydroxy," which appears in the definition of groups R_3, R_4 and R_5 in claims 1 and 2 is indefinite when read in light of the specification. The term is not defined in the specification. Since what constitutes a protecting group for a given functional group depends on the synthetic milieu to which that functional group is to be subjected, the identity of the "protected hydroxy" actually depends on an undefined variable, the type of chemical environment from which the hydroxy group in question is to be protected.

In claim 1, the term "aralkyl" is recited in the definition of groups R_7, R_8 and R_9. Normally, one of ordinary skill would be apprised of what this term denotes, that is, an aryl group bonded to the molecule through an alkylene chain of at least one carbon atom. When the term "aralkyl" is interpreted in light of the instant specification, however, confusion arises because the examples of aralkyl groups provided in section [0044], where the term is defined, include styryl, which is *not* understood normally to be an aralkyl group. Styryl is an arylalkenyl group, since the linking group through which a bond to the core structure would be an alkylene group. Because the examples of

preferred aralkyl groups provided include one aryl-alkenyl group, the term when present as a claim limitation is sufficiently unclear when interpreted in light of the specification to warrant a rejection under the second paragraph of 35 U.S.C. 112. One of ordinary skill, when given the example of a class of substituent not usually understood to be within the meaning of the term aralkyl as being embraced by that term, it is not clear how many other alk**enyl**-aryl groups applicants intend for the term to embrace.

In claim 2, the limitation "wherein n is 0, 1, 2 or 3" is recited, while the claim does not include a variable "n." Thus, there is no antecedent basis in claim 2 for the definition of "n" provided in the latter part of the claim.

Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "prodrug" in claims 6 and 7 renders the full scope of the exclusive right sought by applicants in those claims unclear.

Simply because one of ordinary skill in the art understands what *function* a prodrug serves is not enough to apprise him of which molecular structures lie within the scope of claims 6 and 7 and which lie without. As applicants can appreciate, what is claimed in 6 and 7 is a set of chemical compounds, not a process of administering a drug to an animal by an *in vivo* metabolism process. The specification does not provide any teachings specifically applicable to the allegedly novel compounds disclosed therein which will render the claimed prodrugs. Thus, exactly which compounds are intended

by the "prodrug" language is not readily ascertainable from a reading of claims including that term in light of the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,919,341 (Paruch et al).

Compounds according to claims 1 and 2 would have been obvious to one of ordinary skill given the teachings of Paruch et al at the time the invention was made. Paruch et al discloses kinase inhibitors based on an imidazo[1,2-a]pyrazine core structure, like the compounds according to instant claims 1 and 2. In column 1 and 2, the Paruch et al patent teaches the generic structure of the family of compounds disclosed. The R^1 of Paruch et al corresponds to R_4 of the instant claims; R^2 to R_5; R^3 to R_1 or R_2; R to R_3. Each one of the variables defined in columns 3-5 of the Paruch et al patent is overlapping to some extent with each structural variable set forth in the instant claims.

The deficiency of Paruch et al with respect to the subject matter of claims 1 and 2 is that Paruch et al does not demonstrate the synthesis of a compound bearing a phenyl ring at the 3-position and H at the 5- and 6-positions.

One of ordinary skill, however, motivated by a desire to make the kinase inhibitors disclosed by Paruch et al for therapeutic use or as research tools, would apply the expressly suggested teachings regarding those compounds to the more preferred embodiments of the compounds, which are shown in the examples of the patent. In the examples of Paruch et al, scores of imidazo[1,2-a]pyrazine compounds which are phenyl-substituted at the 6-position (corresponding to "R" in the Paruch et al patent) are disclosed. Most of these compounds are halo-substituted at the 3-position on the bicyclic core (corresponding to "R^2" in the Paruch et al patent). In view of these examples, given the general teachings pertaining to the compounds of that patent, it would have been obvious to one of ordinary skill to simply move the location of the phenyl substituent found in most of the exemplified compounds to the R^2 position on the bicyclic core. Indeed, "aryl" is the third listed possible identity for R^2 in Paruch et al (col. 3, line 42). So, Paruch et al expressly suggests an aryl group at the R^2 position. Additionally, least one exemplified compound in the patent actually *is* phenyl-substituted at the 3-position, which corresponds to R^2 in the patent, and thus, to R_5 in formula (I) of the instant claims – the structure of this compound is depicted at column 89, lines 35-50. It is noted that this compound also bears an aryl group at the 6-position as well, but nonetheless, R^2 in Paruch et al's compounds is expressly suggested to be aryl, and one exemplified compound actually embodies this teaching. It would be obvious, therefore, for one of ordinary skill in the art, to make a 6-phenyl-substituted 8-amino-imidazo[1,2-a]pyrazine compound, given the teaching of Paruch et al. The groups corresponding to

R_3 and R_4 of the instant claims, R and R^1 in the patent, are permitted to be H (col. 3, lines 15 and 40).

All of the substituents on Paruch et al's 8-amino group in the exemplified compounds, save for the pyridyl and pyridylalkyl found on some of the compounds, are permitted in formula (I) of instant claims 1 and 2. Exemplified compounds in the patent are variously substituted on the amino nitrogen atom with (optionally substituted)phenyl, cyclohexyl, acetyl, (substituted)alkyl and aralkyl, to name a few (*e.g.*, col's. 7-14, 42, 45).

Paruch et al expressly suggests to one of ordinary skill in the art of preparative organic chemistry compounds according to instant claims 1 and 2, wherein R_5 is phenyl, one of R_1 and R_2 is H and the other is aryl, aralkyl, heteroalicyclic or substituted alkyl, and R_3 and R_4 are H. Such compounds are clearly in the teaching of Paruch et al.

Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because non-initialed and/or non-dated alterations have been made to the declaration, in the entry for co-inventor Ping Huang. See 37 CFR 1.52(c).

Specification

In the Requirement for Restriction letter mailed prior to this Office action, objection to the abstract of the disclosure was voiced, due to there being no depiction of

a generic structure of the compounds according to the invention. In reply to the objection, applicants' counsel has stated, correctly, that there is no requirement in chemical cases for a structure diagram to appear in the abstract. It is applicants' prerogative whether or not to include a structure diagram of the compounds regarded as the invention. Comments on the abstract were offered because in the examiner's opinion, in chemical cases, an abstract appearing on the face of the printed patent which includes a structure diagram greatly aids in the searching of patent literature, so that examiners and the public can quickly determine if that patent is pertinent to the subject matter in which they are interested.

Because applicants believe the instant invention is sufficiently described by the abstract in its present form, the objection is withdrawn.

Allowable Subject Matter

As noted above in the section headed "Election/Restriction," no claim in the application has been completely searched, due to the nature of Markush practice pursuant to a requirement for an election of species, as set out in the MPEP, chapter 803.02. Compounds according to the instant claims wherein one of R_1 and R_2 is cyclopropyl, R_3 and R_4 are H, R_5 is phenyl, optionally substituted as defined in the instant claims, would be allowable, if the rejections under 35 U.S.C. 112, first and second paragraphs, and the Obviousness-Type Double Patenting rejection are overcome.

Species according to claims 6 and 7, wherein the compound is cyclopropyl substituted at the 8-position on the imidazo[1,2-a]pyrazine core, and phenyl substituted

at the 3-position (substituted in most cases), with no other position on the imidazopyrazine core substituted, are allowable. The examiner counts 28 such compounds in claims 6 and 7. Because the species have not been numbered, it would be too time–consuming to list each allowable specie in claim 6 and claim 7 by name.

The closest prior art with respect to the subject matter indicated as being allowable is the above-cited Paruch et al patent.

Also pertinent are:

US 5,869,485 (Missbach) and US 6,713,474 (Hirst et al), disclosing pyrrolopyrimidine protein kinase inhibitors,

and US 6,919,340 (Currie et al), which discloses imidazopyrazine protein kinase inhibitors.

At such time that the elected subject matter, Group I, that is, is found to be allowable, Group II claims will be rejoined therewith and the Requirement for Restriction previously set forth will be withdrawn. Methods according to instant claims 9-16 will then be the subject of a rejection under the first paragraph of 35 U.S.C. 112, for lack of an disclosure enabling their practice. The examples purportedly showing biological activity of the compounds upon cursory inspection, in the preparation of this Office action, appear to be prophetic; no actual biological data, such as IC_{50} values for the various kinases studies, are reported. Much less is there any concrete nexus between inhibition of a specific kinase and the expansive scope of diseases embraced by the methods in claims 9-16. Upon receipt of a reply to this Office action which obviates all of the rejections set forth herein, the examiner will attempt to contact applicants' counsel

regarding the rejoined claims, so that the necessity for another round of

correspondence may be dispensed with and the application allowed.

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Tuesday-Thursday from 8:00am to 4:30pm or Monday from 6:00am to 1:30pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

zt